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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,832	03/28/2002	Takeshi Nagasu	082370-000000US	8651

7590 11/04/2004

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EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,832	NAGASU ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-8 and 10-22* is/are pending in the application.

4a) Of the above claim(s) *10-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-8,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *1004* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/24/04 has been entered.

2. This action is written in response to applicant's correspondence submitted 8/24/04. Claims 1-4 and 9 have been canceled. Claims 5 and 6 have been amended. Claims 21 and 22 have been added. Claims 5-8 and 10-22 are pending. Claims 10-20 are withdrawn from prosecution. Claims 5-8 and 21-22 are under prosecution herein. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. New rejections are set forth to address applicant's amendments to the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112-Written Description

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 5 is drawn to a method for testing for a cedar pollen allergy, said method comprising conducting hybridization with an RNA sample using a probe comprising nucleotides of gene 513, wherein the nucleotides consist of a segment of nucleotides between positions 36 and 1171 of SEQ ID NO: 1, or the complement thereof.

Claim 6 is drawn to a similar method but employs a PCR using cDNA as a template and a primer comprising comprising nucleotides of gene 513, wherein the nucleotides consist of a segment of nucleotides between positions 36 and 1171 of SEQ ID NO: 1, or the complement thereof.

Claims 7 and 8 depend from claims 5 and 6.

Because the claims are drawn using "comprising" language to describe the primers and probes, the claims encompasses the use of and the detection of sequences that are not described herein, such as full length cDNA, genomic DNA, variants of many forms, nucleic acids from other species of animals, etc. The instant specification specifically sets forth that the language "'nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1' includes the full length gene 513 cDNA (specification p. 9, lines 31-32)."

The large genus of nucleic acids utilized in these methods is represented in the specification by a nucleic acid consisting of instant SEQ ID NO: 1 and nucleic acid fragments consisting of portions of SEQ ID NO: 1. Thus, applicant has express possession of only one species in a genus which comprises many, many different possibilities. The present claims encompass the use and detection of full-length genes and cDNAs that are not fully described,

other than that they contain or hybridize to instant SEQ ID NO: 1 which is a partial cDNA. There is substantial variability among the species of nucleic acid molecules encompassed within the scope of the claims because SEQ ID NO: 1 is only a fragment of any full-length gene or cDNA species. The partial cDNA provided herein does not include a disclosure of an open reading frame of which it is a part is not representative of the genus of cDNAs and genes encompassed by the claims because no information regarding the coding capacity of the any cDNA molecule is disclosed. Since the claimed genus encompasses genes yet to be discovered, the disclosed structural feature does not constitute a substantial portion of the claimed genus.

With regard to the written description, all of these claims encompass nucleic acid sequences or methods which utilize nucleic acid sequences different from those disclosed in the specific SEQ ID No:s which, for claims 5-8 include modifications allowed by the hybridization language for which no written description is provided in the specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only a nucleic acid consisting of instant SEQ ID NO: 1 and nucleic acids consisting of fragments of instant SEQ ID NO: 1 are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

Weighing all factors, including the partial structure of the DNAs that comprise fragments of SEQ ID NO: 1, the breadth of the claims as reading on any number of undescribed nucleic acids, and the lack of correlation between the structure and function of the genes and cDNAs that are not described, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of DNAs which comprise SEQ ID NO: 1 or which hybridize to SEQ ID NO: 1, as encompassed by and/or used in the instant product and method claims.

Claim Rejections - 35 USC § 112-Scope of Enablement

Claims 5-8 and 21-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the methods as recited for the testing of cedar pollen allergies in humans, and hybridization methods wherein the probe consists of a fragment of SEQ ID NO: 1, does not reasonably provide enablement for methods wherein the probe consists of the complement of a fragment of SEQ ID NO: 1 or for methods of testing for a cedar pollen allergy in non-human subjects. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature of the Invention and Breadth of the Claims

The invention provides a method for testing for allergic disease which utilizes the detection of a differentially expressed cDNA molecule in a sample of RNA isolated from T cells. The rejected claims encompass the detection of any cedar pollen allergy in any subject, including humans as well as other species of animal, for example dogs or cats. Furthermore, with regard to

claims 5, 8, and 21, the claims encompass using disease, including pet allergies, food allergies, dust mite allergies, allergies to any type of pollen, etc.

Guidance in the Specification and Working Examples

The specification teaches that instant SEQ ID NO: 1 is differentially expressed in human patients that suffer from cedar pollen allergy as compared to those that do not (Example 6, p. 20). The specification demonstrates that a significantly higher level of SEQ ID NO: 1 expression was seen in an group of cedar pollen allergy sufferers (high IgE group) when compared to a control group (Table 5 and Fig. 2). In order to demonstrate that the allergy reaction being tested is indeed cedar pollen reaction, the specification uses as control variables for comparison cypress pollen and two types of house dust mites (Table 2). The specification does not provide any additional guidance as to other species of subjects which may express instant SEQ ID NO: 1 or whether or not this particular gene fragment may be an indicator of pollen allergy in additional species of animals.

Further, with regard to claims 5, 8, and 21, these claims are drawn to methods of testing for a cedar pollen allergy, and recite a step of conducting hybridization with an RNA sample using a probe comprising nucleotides of gene 513, wherein the nucleotides consist of a segment of nucleotides between positions 36 and 1171 of SEQ ID NO: 1, or the complement thereof. Instant SEQ ID NO: 1 is a cDNA (complementary DNA) molecule that was obtained by reverse transcription of an mRNA isolated from a human sample. However, RNA is a single stranded molecule, and so it is not possible that both SEQ ID NO: 1 and the complement of SEQ ID NO: 1 would hybridize to the RNA in a sample. In the instant case, it would only be possible for

fragments of SEQ ID NO: 1 itself, which is complementary to the expressed mRNA to hybridize to the RNA in the sample required in claim 5.

State of the Art

Instant SEQ ID NO: 1 is a novel sequence. The prior art does not provide any guidance as to whether or not instant SEQ ID NO: 1 is expressed in other allergy suffering animals, nor whether or not this sequence is an indicator of allergies in these animals.

Skill in the Art and Unpredictability, and, Quantity of Experiment

While the level of skill in the relevant art is quite high, the unpredictability with regard to the instantly claimed invention is higher. It is entirely unpredictable which other species of animal might be tested for using an assay for the detection of expression of SEQ ID NO: 1 in light of the fact that the expression of a gene comprising SEQ ID NO: 1 or fragments of SEQ ID NO: 1 in subjects of other species is entirely unknown. This is especially highlighted by the instant specification which uses two other dust mite allergens and a different pollen allergen as controls in the experiments for establishing the utility of instant SEQ ID NO: 1 as an indicator of cedar pollen allergy. The practice of the claimed invention commensurate in scope with the broad claims would require an extremely large amount of experimentation wherein subjects of additional species (for example, dogs or cats) with cedar pollen allergy are screened and tested to determine whether or not instant SEQ ID NO: 1 is in fact a marker for cedar pollen allergy in additional species of animals.

Conclusion

Thus, having carefully considered each of these factors, it is concluded that it would require undue experimentation to make and use the claimed invention commensurate in scope

with the instant claims which are directed towards testing for cedar pollen allergy in any species of animal, and for claims 5, 8, and 21 which are drawn to using both the complement of SEQ ID NO: 1 and SEQ ID NO: 1 (or fragments thereof) for the detection of a single stranded RNA molecule via hybridization.

Claim Rejections - 35 USC § 112- New Matter

4. Claims 5-8 and 21-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the new limitation of "nucleotides 36-1171 of SEQ ID NO: 1" in claims 4-8 and 21-22 appears to represent new matter. The remarks filed with the amendment state that the first 35 nucleotides of SEQ ID NO: 1 correspond to a primer and adaptor sequences used in the isolation of SEQ ID NO: 1, and cites a portion of the specification that states "the adaptor primer" provided in a Marathon cDNA Amplification kit was used." However, this is not sufficient to provide basis for the newly added range. The specification does not identify the length of the adaptor primer. The two adaptor primers taught in the user manual provided by applicant are a 27 and 23 base pairs long. It is not clear from the teachings of the specification that nucleotides 1-35 of SEQ ID NO: 1 are the "adaptor primer" referred to in the specification. Therefore the claims are rejected as containing new matter.

Response to Remarks

Written Description Rejection

Applicants have amended claims 4-8 to recite that the probe (or primers) are fragments of gene 513 "comprising nucleotides of gene 513, wherein the nucleotides consist of a segment..." Applicant argues that in this language the first transitional term "comprising" leaves the probe or primer open to sequences unrelated to gene 513 (see Remarks, p. 8, final paragraph). This is correct, but it is also correct that the use of the term "comprising" leaves the probe or primer open to sequences related to gene 513. There is no support in the specification for applicant's limited reading of the scope of the term "comprising." Therefore, the written description rejection is maintained for the reasons of record. If applicant is able to identify support in the specification for an amendment to that recites flanking sequences unrelated to gene 513, such an amendment may be helpful to overcome this rejection. However, the examiner was not able to identify support in the specification for such an amendment, and so, applicant is advised to identify specific support if any such amendment is added to the claims in order to avoid the issue of new matter.

Enablement Rejection

A newly set forth enablement rejection is included in this office action to address the probe of claims 5, 8, and 21, as well as the scope of all of the claims which include the examination of non-human subjects.

New Matter Rejection

The new matter rejection is maintained, and applied to newly added claims 21 and 22. Applicants argue that the limitation "between positions 36 and 1171 of SEQ ID NO: 1" is

supported in the specification by the teaching that "the adaptor primer" provided in a Marathon cDNA Amplification kit was used." However, this is not sufficient to provide basis for the newly added range. The specification does not identify the length of the adaptor primer. The two adaptor primers taught in the user manual provided by applicant are a 27 and 23 base pairs long, not 35 base pairs long. In response to the new matter rejection, applicant has provided the user manual for the Marathon cDNA amplification kit, and further pointed out that the first nucleotides of instant SEQ ID NO: 1 are identical to the 23 nucleotides of Nested Adaptor Primer 2 of the Maration kit plus 12 nucleotides from the Marathon cDNA Adaptor immediately 3' to the binding site for Nested Adaptor primer 2. The specification does not provide this teaching. The specification provides no suggestion that instant SEQ ID NO: 1 comprises particular ranges that are preferred for selection of probes and primers. The specification contains no discussion of which portions and sequences from the marathon kit or user manual were utilized. Therefore, the rejection for new matter is maintained.

Applicant is advised that the removal of the range from the claims, so that the claims recite a probe or primers consisting of all or a fragment of SEQ ID NO: 1 (or the complement of SEQ ID NO: 1 for the primers of claim 6) would overcome the new matter rejection and the written description rejection. Such a claim would encompass non-functional embodiments, for example a probe consisting of nucleotides 1-35 of SEQ ID NO: 1, however, the selection of functional embodiments within the scope of such a claim would be entirely within the skill of the art. Furthermore, amendment of the claims to recite that the subject is a human, in combination with the previously suggested amendment to define the probe or primers would overcome the scope of enablement rejection.

Prior to allowance, the cancellation of non-elected claims 10-20 will also be required.

Conclusion

5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached by calling (571) 272-0745.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

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Juliet C. Switzer
Examiner
Art Unit 1634

November 3, 2004